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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/049,745	01/30/2002	Henry Yue	PF-0727 USN	6011

22428 7590 09/07/2004

FOLEY AND LARDNER
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WASHINGTON, DC 20007

EXAMINER

SCHNIZER, HOLLY G

ART UNIT	PAPER NUMBER
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1653

DATE MAILED: 09/07/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/049,745

Applicant(s)

YUE ET AL.

Examiner

Holly Schnizer

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 July 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-11,13,15-17,19,22,25,26 and 28 is/are pending in the application.
- 4a) Of the above claim(s) 8,10,13,15,22,25,26 and 28 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-7,9,11,16,17 and 19 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of the Claims

The Preliminary Amendment filed January 30, 2002 has been entered. Claims 12, 14, 18, 20, 21, 23, 24, and 27 have been cancelled. Therefore, Claims 1-11, 13, 15-17, 19, 22, 25-26, and 28 are pending. Claims 8, 10, 13, 15, 22, 25-26, and 28 are withdrawn from consideration as being drawn to non-elected subject matter. And, Claims 1-7, 9, 11, 16, 17, and 19 have been considered on the merits to the extent that they relate to SEQ ID NOs: 4 and 31.

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-7, 9, 11, 16-17, and 19 and SEQ ID NO: 31 encoding the polypeptide of SEQ ID NO:4 in the reply filed on July 28, 2004 is acknowledged. The traversal is on the ground(s) that MPEP 804.03 requires that ten distinct polynucleotide sequences be searched in a single application. This is not found persuasive because the policy stated in the Examination of Patent Applications Containing Nucleotide Sequences, 1192 O.G. 68 (November 19, 1996), is intended to limit restrictions among EST sequences where "normally ten sequences constitute a reasonable number for examination purposes". As stated in the Restriction Requirement each of the polynucleotides that Applicant requests to be rejoined with Group I encode structurally and functionally distinct products that have no similarity in their primary, secondary, or tertiary structures. And, there is no apparent shared common core structure or apparent shared art recognized function and thus the

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sequences are patentably distinct. Furthermore, a search of more than one of the patentably distinct sequences of the invention would be unduly burdensome since they have entirely different structures and functions.

Therefore, the requirement is still deemed proper and is therefore made FINAL.

Priority

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)). The specific reference to any prior nonprovisional application must include the relationship (i.e., continuation, divisional, or continuation-in-part) between the applications except when the reference is to a prior application of a CPA assigned the same application number.

Objections to the Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (e.g. p. 50, line 20). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01(VII).

This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Claim Objections

The claims are objected to for the following informatlities: Claims 1-7, 9, 11, 16, 17, and 19 are objected to because they encompass sequences which are non-elected. Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-7, 9, 11, 16, 17, and 19 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility. Since a specific and substantial utility has not been found, credibility has not been assessed.

A search of the sequence and text databases appears to indicate that the claimed polynucleotides and polypeptides do not have a well-established utility.

The Specification asserts that the polynucleotides and polypeptides of the invention have specific utilities including methods of treatment, diagnosis, methods of drug screening, methods of detecting single nucleotide polymorphisms (SNPs), in microarrays to monitor relative expression of a large number of genes simultaneously or to monitor protein-protein interactions, drug-target interactions, or to map the chromosome.

The Specification discloses that the protease of SEQ ID NO: 4 has sequence similarity to ubiquitin carboxyl terminal hydrolase family of proteins. The specification

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merely proposes that the polynucleotides and polypeptides disclosed therein could be used for the diagnosis, treatment, and prevention of a large number of diseases, disorders, and conditions, many of which are unrelated and, that occur in various tissues and in the assessment of the effects of exogenous compounds on the expression of nucleic acid and amino acid sequences of the proteases. The specification discloses 27 different polypeptide sequences that appear to have different functions and 27 polynucleotide sequences that encode those polypeptides and the specification does not teach how any one of these polypeptides or polynucleotides relates to a specific disease. Thus, this proposal is considered an invitation to further experimentation to determine a specific and substantial utility for the claimed polynucleotide and polypeptide because the specification does not provide guidance as to how any one of the disclosed polynucleotides or polypeptides relates to any specific disease and provides no suggestion of a physiological or cellular function for the claimed polypeptide or the polynucleotide encoding it. A method of using a material for further research to determine, e.g. its specific biological role, thus identifying or confirming a "real world" context for its use, cannot be considered to be a "substantial utility". *Brenner v. Manson*, 383 U.S.519, 148 USPQ 689 (Sup. Ct. 1966). Mere allegations of a prospective, potential utility cannot rise to the level of a specific in vivo utility that is substantial.

The asserted utility that the claimed polynucleotides and/or polypeptides can be used for drug screening, in microarrays, to determine toxicity of test compounds, to map the chromosome, and to detect SNPs are not considered specific. These asserted

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utilities are not considered specific because they are not specific to the claimed polynucleotides. For example, any polynucleotide could be used in a microarray or to screen for some sort of pharmaceutical agent (drug). Likewise, absent any information regarding the specific location of the claimed polynucleotide on the chromosome and absent any specific DNA target, any polynucleotide could be used as a chromosome marker.

The asserted utility that the claimed polypeptides can be used in microarrays to analyze protein-protein or drug-target interactions is not considered specific or substantial. The asserted utility is not considered specific because any polypeptide could be used in a protein-protein binding assay. It is not considered substantial since, with the lack of information regarding the claimed polypeptide biochemical and/or physiological function, it amounts to basic research for studying the properties of the claimed product itself. (see Utility Guidelines Training Materials available at www.USPTO.gov, p. 6).

The assertion that the claimed polypeptides could be used to screen agonists and antagonists is also not considered specific or substantial. This assertion is not considered specific because every protein has an agonist and antagonist and thus could be used to screen for such agents. The assertion is not considered substantial since the Specification does not provide any guidance with respect to the physiological function of the claimed polypeptide or with respect to the identity of any agonists or antagonists, or their physiological function. Thus, the asserted utility amounts to a

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method of assaying or identifying a material that itself has no specific or substantial utility (see Utility Guidelines Training materials available at www.USPTO.gov, p. 6).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7, 9, 11, 16, 17, and 19 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim 1, 3, 6, 7, 9, 16, 11, and 19 are further rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement for the following reasons. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re Wands* (858 F2d, 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). These factors include (1) quantity of experimentation, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in

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the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The nature of the invention involves the isolation of cDNA molecules encoding proteins that share sequence similarity with proteases and protease inhibitors. The Specification discloses 27 unique sequences that appear to have unique functions. The claimed polypeptide has sequence similarity to the proteins in the ubiquitin carboxyl terminal hydroxylase family. The specification does not provide any further guidance as to the function of the claimed polypeptide or the polynucleotide encoding it or the parts of the sequence that were essential for "biological activity" or the parts of the sequence that were immunogenic. There are no working examples concerning the polypeptide or polynucleotide encoding it.

The breadth of the claims encompasses any polypeptide sequence that is at least 90% identical to SEQ ID NO:4 (clms 1b), any "biologically active fragment" of SEQ ID NO:4 (clm. 1c), any "immunogenic fragment" of SEQ ID NO:4 (clm. 1d), any polynucleotide encoding the sequences of claim 1 and any host cell containing such a polynucleotide (clms. 3, 6, 7), a method of making the polypeptides (clm. 9), compositions comprising the polypeptides (clm. 16), and methods of using any of the polypeptides (clm. 19).

The state of the prior art is such that it does not supplement the information lacking in the Specification concerning the function of the polypeptide of SEQ ID NO:4. Ubiquitin carboxyl terminal hydrolases appear to have been known in the art at the time of filing the present application, however it appears that these proteins were not well

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characterized (Sun et al. (Cell Research (2002) 12(3-4): 199-206). Thus, the relative skill of those in the art was not at the level that one could look at a ubiquitin carboxyl terminal hydrolase and, without testing for its activity, predict which parts of the sequence were essential to biological activity and which were not or predict which parts of the sequence were immunogenic.

The art of predicting protein function based solely on amino acid sequence is highly unpredictable. One cannot merely predict protein function from amino acid sequence information or from amino acid sequence similarity to other related proteins. While it is known that many amino acid substitutions are generally possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions (see Bowie et al., 1990, Science 247:1306-1310, especially p.1306, column 2, paragraph 2; Wells, 1990, Biochemistry 29:8509-8517; Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure, pp. 14-16). Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which

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conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity.

A large quantity of experimentation would be required to characterize the claimed protein and polynucleotide encoding it to determine which amino acid residues could be altered. To make the claimed polynucleotides and polypeptides would not require just a repetition of work that is described in the instant application but a substantial inventive contribution on the part of a practitioner which would involve the characterization of the amino acid residues which are essential to biological activity and which are involved in immune recognition. It is this additional characterization of the polynucleotide and encoded protein that constitutes undue experimentation.

Claims 1, 3, 6, 7, 9, 16, 11, and 19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a "written description" rejection, rather than an enablement rejection under 35 U.S.C. 112, first paragraph. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, first paragraph "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-111, Friday January 5, 2001.

Vas-Cath Inc. V. Mahurka, 19 USPQ2d 1111, states that “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention, for purposes of the “written description” inquiry, is *whatever is now claimed*” (see page 1117).

A review of the claims indicates that these claims are drawn to a genus, i.e., Claim 1(b) is drawn to a genus of polypeptides having at least 90% sequence identity to SEQ ID NO:4, Claim 1(c) is drawn to the genus of biologically active fragments of SEQ ID NO:4, Claim 1(d) is drawn to immunogenic fragments of SEQ ID NO:4, Claims 3, 6, 9, 16, and 19 are drawn to polynucleotides encoding and host cells containing the polynucleotides encoding, methods of making, compositions comprising, methods of screening compounds using the genus of polypeptides of claim 1. Claim 11(b) is drawn to a genus of polynucleotide sequences that are at least 70% identical to SEQ ID NO: 31 and Claim 11(d) and (e) are drawn to the genus of sequences that are complementary or equivalent to the sequences of claim 11(b).

A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In *Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that,

while applicants are not required to disclose every species encompassed by a genus, the description of the genus is achieved by the recitation of a representative number of species falling within the scope of a the claimed genus. At section B(1), the court states "An adequate written description of a DNA...requires a precise definition, such as by structure, formula, chemical name, or physical properties, not a mere wish or plan for obtaining the claimed chemical invention".

There is a single species of the claimed genus disclosed that is within the scope of the claimed genus, *i.e.* the polypeptide having the sequence of SEQ ID NO:4 and the polynucleotide of SEQ ID NO:31 that encodes the polypeptide. The disclosure of a single species may provide an adequate written description of a genus when the species disclosed is representative of the genus. However, the present claim encompasses numerous species that are not further described. There is substantial variability among the species.

One of skill in the art would not recognize from the disclosure that the applicant was in possession of the genus which comprises sequences at least 90% identical to SEQ ID NO: 4, biologically and immunologically active fragments of SEQ ID NO:4, sequences at least 70% identical to SEQ ID NO: 31, polypeptides encoded by these sequences, or methods of using or making these sequences . The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (see *Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 11 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 11(e) recites "an RNA equivalent of a)-d)". Since it is unclear as to how RNA could be equivalent to all of a)-d), this language is confusing as to whether the RNA must be equivalent to all of a)-d) as the claim suggests or if it was intended to be equivalent to any one of a)-d). Clarification is required.

Conclusions

No Claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Holly Schnizer whose telephone number is (571) 272-0958. The examiner can normally be reached on Monday through Wednesday from 8 am to 5:30 pm.

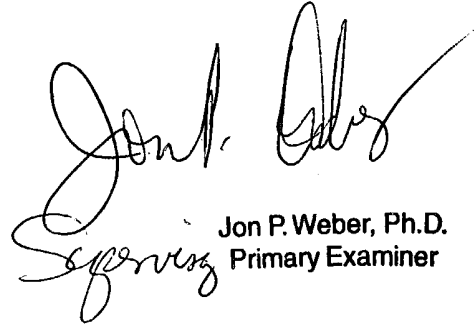
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on (571) 272-0925. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Holly Schnizer
August 25, 2004



Jon P. Weber, Ph.D.
Primary Examiner